Type of Treatment and Short-Term Outcome in Elderly Patients With Acute Myocardial Infarction Admitted to Hospitals With a Primary Coronary Angioplasty Facility. The TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) Registry

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Introduction and objectives. The nature and outcome of treatment for acute myocardial infarction in elderly patients admitted to Spanish hospitals with primary angioplasty facilities are not well documented.

Patients and method. Prospective analysis of registry data on patients ≥75 years old with ST-segment-elevation acute myocardial infarction admitted between April and July 2002 to Spanish hospitals with an active primary angioplasty program.

Results. We followed up 410 consecutive patients for 1 month. Their mean age was 80 (4.3) years and 46% were female. The median delay between symptom onset and arrival at hospital was 190 minutes. Around 42% of patients received no reperfusion therapy, 35% were treated by thrombolysis, and 22% by primary angioplasty. Patients who underwent reperfusion therapy were younger, were more frequently male, had a shorter delay from symptom onset to hospital arrival, and had a better initial hemodynamic status (Killip Class). However, they were more likely to have extensive anterior infarctions. Overall, 30-day mortality was 24.9%. Independent predictors of death were age, systolic blood pressure, and Killip class >1, but not use of thrombolysis or primary angioplasty.

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*The researchers and hospitals participating in the TRIANA 1 and 2 subregistries are listed in the Appendix.

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Conclusions. Over 42% of elderly patients with myocardial infarction admitted to Spanish hospitals with angioplasty facilities did not receive reperfusion therapy. Thrombolysis was the most frequently used reperfusion therapy. However, neither thrombolysis nor primary angioplasty improved 30-day mortality.

Key words: *Myocardial infarction. Population study. Thrombolysis. Primary angioplasty. Registry data. Reperfusion. Prognosis.*

Tratamiento y evolución a corto plazo de los ancianos con infarto agudo de miocardio ingresados en hospitales con disponibilidad de angioplastia primaria. El Registro TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos)

Introducción y objetivos. Se desconoce cómo son tratados y cómo evolucionan los pacientes ancianos con infarto agudo de miocardio atendidos en hospitales españoles que realizan angioplastia primaria (AP).

Pacientes y método. Registro prospectivo de pacientes ≥ 75 años ingresados por infarto agudo de miocardio con elevación del segmento ST en hospitales españoles que tienen un programa activo de AP (abril-julio de 2002).

Resultados. Se estudió a 410 pacientes consecutivos con un seguimiento de 1 mes. La edad media fue de 80 ± 4,3 años y un 46% era mujer. La mediana de retraso desde el inicio de los síntomas a la llegada al hospital fue de 190 min. El 42% de los pacientes no recibió tratamiento de reperfusión, el 35% fue tratado con trombólisis y el 22% con angioplastia primaria. Los pacientes que recibieron tratamiento de reperfusión eran más jóvenes, con más frecuencia varones, llegaron con menor retraso desde el inicio de los síntomas al hospital, tenían una situación hemodinámica inicial (clase Killip) más favorable, pero se trataba con mayor frecuencia de infartos anterio-

ABBREVIATIONS

PA: primary angioplasty.
AMI: acute myocardial infarction.
LVEF: left ventricular ejection fraction.
BP: blood pressure.

res y más extensos. La mortalidad a los 30 días fue de 24,9%; fueron predictores independientes de ella la edad, la presión arterial sistólica y la clase de Killip > 1, pero no el uso de fibrinolíticos ni de AP.

Conclusiones. El 42% de los ancianos con infarto agudo de miocardio que ingresan en hospitales españoles con programa de AP no recibe tratamiento de reperfusión. La fibrinólisis fue el tratamiento de reperfusión más empleado. La fibrinólisis y la AP no se asociaron con mejoría del pronóstico de mortalidad a los 30 días.

Palabras clave: *Infarto de miocardio. Población. Fibrinólisis. Angioplastia primaria. Registro. Reperfusión. Pronóstico.*

INTRODUCTION

Elderly acute myocardial infarction (AMI) patients present specific clinical characteristics which differ from younger patients. These include a higher proportion of women, high comorbidity, longer delay before using the emergency service, and very high hospital and short-term mortality.[1-6] Despite the poor prognosis, very elderly patients, ≥75 years old, normally receive less aggressive or complete medical treatment.[1] Furthermore, the efficacy of reperfusion therapy in these patients remains a matter of dispute. This is particularly true regarding fibrinolysis.[7-10] On the other hand, there is little data regarding the advantages of primary angioplasty (PA) versus fibrinolysis.[11-13] For these reasons, the need for a randomized study comparing both therapeutic choices is patent.[13] The Ischemic Cardiopathy and Hemodynamics Sections of the Spanish Society of Cardiology, being aware of this need, considered it necessary to investigate the clinical characteristics, treatment and prognosis of elderly AMI patients admitted to Spanish hospitals with an active PA program. The final aim was to study the feasibility of carrying out a national clinical trial comparing fibrinolysis and PA in these patients. Thus, the TRatamiento del Infarto Agudo de miocardio eN Ancianos (TRIANA) Registry was set up and divided into 2 subregistries: TRIANA 1, which included all the AMI patients of any age who underwent PA or rescue angioplasty, and TRIANA 2, which included all the patients >75 years old who did not undergo early coronary angioplasty (primary or rescue). This paper presents the outcomes of the patients ≥75 years old included in both registries.

PATIENTS AND METHODS

Patients

The TRIANA Registry is a prospective multicenter study in which all the Spanish hospitals that performed a minimum of 50 PA per year were invited to participate. A total of 26 centers accepted the invitation (1 hospitals did not include patients in TRIANA 1 and 1 did not include them in TRIANA 2). Between 18 March and 31 July 2002, the TRIANA 2 subregistry included all the patients ≥75 years old admitted with ST-segment elevation AMI or complete left branch bundle block who did not receive PA or rescue angioplasty. The TRIANA 1 subregistry included 459 patients on similar dates but with 1 month less recruitment time. In the present article the data from the 306 patients included in the TRIANA 2 subregistry are analyzed plus those from the 104 patients ≥75 years old included in the TRIANA 1 subregistry (92 received PA and 12 rescue angioplasty).

Variables

The variables analyzed were: *a)* baseline and demographic characteristics (Table 1); *b)* infarction characteristics (Table 2); *c)* medical treatment (Table 3); *d)* diagnostic tests: echocardiography, non-invasive ischemia detection tests (ergometry, echocardiography stress test or tests with radioactive isotopes), emergency or elective catheterization, and angioplasty; *e)* hospital evolution (Table 4); and *f)* 30-day follow-up.

Statistical Analysis

The results of the continuous variables are expressed as mean±SD, or as median and 25/75 percentiles when they did not follow a normal distribution. The means between the three groups were compared with ANOVA. Between-group categorical variables were compared with the χ^2 test. The predictive value of the variables contributing to mortality was analyzed using a multiple logistic regression model constructed by introducing all the variables with a significant relationship to mortality ($P<.1$). Subsequently, those which did not contribute additional information to the model were excluded step-by-step. In addition, the variable reperfusion was introduced (although not in contrast to fibrinolysis/PA). All the analyses were done with SPSS software version 11.0 (SPSS, Inc., 2002) and expressed as 2-tailed *P*-values. Mortality risk was adjusted for age, sex, systolic blood

TABLE 1. **Risk Factors and Background***

	Without Reperfusion (n=172)	Fibrinolysis (n=146)	Angioplasty (n=92)	*P*
Age	81.5±4.6	79.8±4	79.4±3.8	<.0001
Women	97 (56.4)	66 (45.2)	27 (29.3)	<.0001
Risk factors				
Hypertension	116 (69.5)	84 (58.7)	60 (69)	.10
Hyperlipidemia	53 (34.2)	43 (32.1)	28 (33.3)	.93
Diabetes	58 (34.5)	39 (27.7)	30 (33.7)	.40
Insulin treatment	17	15	4	.08
Smoking habit				
Current smoker	12 (7.3)	20 (14.7)	14 (16.5)	.002
Previous smoker	38 (23.2)	44 (32.4)	33 (38.8)	.002
Never smoked	114 (69.5)	72 (52.9)	38 (44.7)	.002
Previous ischemic heart disease				
Myocardial infarction	34 (20.4)	22 (15.4)	20 (21.7)	.39
Unstable angina	43 (25.7)	30 (20.8)	26 (29.2)	.32
Stable angina	27 (16.3)	19 (13.4)	11 (12.1)	.61
Coronary angioplasty	8 (4.7)	8 (5.5)	11 (12.1)	.057
Coronary surgery	7 (4.1)	3 (2.1)	2 (2.2)	.51
Cardiovascular background				
Heart failure	17 (10.1)	7 (4.9)	4 (4.4)	.10
Stroke	23 (13.6)	16 (11.1)	13 (14.1)	.73
Peripheral vasculopathy	17 (10.3)	9 (6.3)	6 (6.5)	.36
Other background				
Chronic kidney failure	20 (12.0)	4 (2.8)	2 (2.2)	.01
Dementia	9 (5.3)	4 (2.8)	1 (1.1)	.17
Daily activity				
Autonomous	118 (69.0)	116 (80.6)	70 (76.9)	.002
Partial dependency	42 (24.6)	25 (17.4)	10 (11.0)	.002
Total dependency	11 (6.4)	3 (2.1)	11 (12.1)	.002

*Values are expressed as number of cases and percentage of total numbers (n).

pressure at the time of admission, fibrinolysis, PA, Killip class and AMI location.

RESULTS

Characteristics of the Population

Four hundred and ten patients were recruited over 4.5 months. Mean age was 80±4.3 years (range, 75-98 years) and 46.3% were women. Out of the total, 146 (35.6%) received fibrinolytic treatment—12 of whom (9%) also underwent rescue angioplasty—, 92 (22.4%) PA, and 172 (42%) did not undergo any type of reperfusion therapy. Treatment was decided according to the criterion of the acting specialist and the current protocol in each hospital. The majority of the patients treated with fibrinolytics (86.9%) received the drug in the first 6 h from onset of symptoms; tenecteplase was the most frequently administered agent. No reason was given for non-administration of fibrinolytic therapy in 21.6% of cases, whereas in the remainder the researchers considered that there was some type of contraindication (51.1% delayed admission, 12.4% advanced age, 10.9% comorbidity, 5.8% hemorrhagic risk, 1.5% previous stroke, and 18.2% other causes).

The patients who received reperfusion therapy, versus those who did not, were younger, presented pain as the main symptom and anterior AMI more often, were admitted with less delay and presented fewer signs of pulmonary congestion. Furthermore, there were fewer women and less background of kidney failure or dependency during daily activities. Tables 1 and 2 show differences in baseline and AMI characteristics between the 3 groups of patients.

Patients receiving some type of reperfusion therapy were more often treated with heparin, clopidogrel, glycoprotein IIb/IIIa inhibitors, beta-blockers, and ACE inhibitors, whereas those who did not receive reperfusion therapy required diuretics more often. Table 3 shows the between-group differences.

The patients who did not receive reperfusion therapy presented a higher incidence of heart failure and postinfarction angina, a trend toward greater incidence of shock and mechanical complications, but less stroke (1.2 vs 4.2%; *P*=.07) and hemorrhage (2.9 vs 8.8%, *P*=.02). The incidence of stroke was slightly higher in the group treated with fibrinolytics (six out of the eight cases involved hemorrhagic stroke). Table 4 shows evolution according to type of treatment. Echocardiogram was done in 75.1% of

TABLE 2. **Infarction Characteristics***

	Without Reperfusion (n=172)	Fibrinolysis (n=146)	Angioplasty (n=92)	*P*
Delay from onset of symptoms until hospital admission				
<6 h	66 (40.0)	126 (86.9)	73 (83.9)	<.0001
6.1-12 h	40 (24.2)	16 (11.0)	13 (14.9)	<.0001
12.1-24 h	39 (23.6)	2 (1.4)	1 (1.1)	<.0001
>24 h	20 (12.1)	1 (.7)	0	<.0001
Time onset symptoms-hospital, min†	300 (129-696)	180 (111-270)	150 (85-255)	<.0001
Time door-beginning reperfusion, min†	–	49 (30-88)	90 (60-143)	<.0001
Time onset symptoms-beginning reperfusion, min	–	240 (160-330)	234 (180-415)	.11
Electrocardiographic location‡				
Anterior	62 (36.0)	69 (47.3)	56 (60.9)	.001
Inferior	76 (44.2)	68 (46.6)	32 (34.8)	.18
Lateral	32 (18.6)	43 (29.5)	32 (34.8)	.009
Posterior	25 (14.5)	25 (17.1)	19 (20.7)	.44
Indeterminate	28 (16.3)	3 (2.1)	1 (1.1)	<.0001
Complete right bundle branch block	15 (8.8)	17 (11.8)	9 (9.8)	.67
Complete left bundle branch block	19 (11.3)	7 (4.8)	2 (2.2)	.01
Right ventricular disease	12 (7.1)	20 (13.8)	11 (12.0)	.13
Q-wave development	126 (73.3)	117 (81.3)	72 (79.1)	.21
Killip class III or IV at admission	51 (29.8)	18 (12.3)	15 (15.2)	<.0001
Maximum CK, U/L†	774 (424-1230)	1576 (965-3042)	1512 (698-2779)	<.0001
Maximum CK-MB, U/L†	85 (41-161)	206 (139-371)	224 (121-370)	<.0001

*CK indicates creatine kinase; CK-MB, creatine kinase MB isoenzyme. Values are expressed as number of cases and percentage of total numbers (n).
†Mean (25/75% percentiles).
‡Non-exclusive.

TABLE 3. **Medical Treatment***

	Without Reperfusion (n=172)	Fibrinolysis (n=146)	Angioplasty (n=92)	*P*
Antithrombolytic therapy				
Aspirin	163 (94.8)	143 (98.6)	90 (97.8)	.12
Clopidogrel/ticlopidine	36 (20.9)	35 (24.3)	82 (89.1)	<.0001
Unfractionated heparin	45 (26.2)	57 (39.6)	25 (27.2)	.02
Low-molecular-weight heparin	121 (70.3)	90 (62.5)	41 (45.1)	<.0001
Glycoprotein IIb/IIIa inhibitors	11 (6.4)	11 (7.6)	44 (47.8)	<.0001
Other drugs				
Nitroglycerin IV	120 (69.8)	107 (73.8)	55 (60.4)	.09
Beta-blockers IV	9 (5.2)	14 (9.7)	2 (2.2)	.05
Oral beta-blockers	79 (45.9)	75 (51.7)	54 (58.7)	.13
Nitrates	86 (50.0)	62 (43.1)	33 (35.9)	.08
ACE inhibitors	117 (68.0)	103 (71.0)	57 (62.0)	.34
Calcium antagonists	19 (11.2)	11 (7.6)	11 (12.1)	.45
Diuretics	106 (61.6)	64 (44.4)	34 (37.0)	<.0001
Inotropics	46 (26.9)	28 (19.4)	24 (26.1)	.26
Digoxin	23 (13.4)	10 (7.0)	14 (15.2)	.10

*IV indicates intravenous. Values are expressed as number of cases and percentage of total numbers (n).

the patients, with a left ventricular ejection fraction lower than 0.40 in 32%. A screening test for ischemia (ergometry, echocardiography stress test or tests with radioactive isotopes) was only done in 13% of the patients. Elective catheterization was done in 18%.

Hospital and 30-Day Mortality

Global hospital mortality was 24.1%, mainly due to cardiogenic shock (58.6%). There were no differences in hospital mortality regarding reperfusion therapy (22 vs 26.7%; *P*=.30), although the cause of death differed

TABLE 4. **Hospital Evolution***

	Without Reperfusion (n=172)	Fibrinolysis (n=146)	Angioplasty (n=92)	*P*
Heart failure				
Pulmonary congestion	66 (38.4)	48 (33.3)	27 (29.3)	.31
Killip class III or IV	68 (39.5)	33 (23.0)	21 (22.8)	.001
Cardiogenic shock	39 (22.7)	22 (15.3)	15 (16.5)	.20
Mechanical complications	8 (4.7)	5 (3.5)	2 (2.2)	.59
LV free wall rupture	5 (2.9)	3 (2.1)	1 (1.1)	.65
Interventricular communication	3 (1.7)	1 (.7)	0	.35
Ruptured papillary muscle	0	1 (.7)	1 (1.1)	.44
Ischemic/vascular complications				
Postinfarction angina	25 (14.5)	25 (17.1)	3 (3.3)	.006
Reinfarction	6 (3.5)	4 (2.7)	1 (1.1)	.51
Stroke	2 (1.2)	8 (5.5)	2 (2.2)	.06
Hemorrhage	5 (2.9)	10 (6.8)	11 (12.0)	.01
Hematoma	8 (4.7)	11 (7.5)	7 (7.6)	.49
Transfusion	9 (5.2)	3 (2.1)	8 (8.7)	.06
Arrhythmias				
Atrial fibrillation	33 (19.2)	28 (19.4)	19 (20.7)	.95
Sustained ventricular tachycardia	6 (3.5)	10 (6.9)	8 (8.7)	.18
Primary ventricular fibrillation	6 (3.5)	9 (6.3)	6 (6.6)	.42
Atrioventricular blockage	10 (5.8)	16 (11.3)	6 (6.5)	.15
Pacemaker	11 (6.4)	12 (8.4)	4 (4.3)	.47
Other complications				
Infection	19 (11.0)	21 (14.5)	9 (9.8)	.49
Agitation/confusion	25 (14.5)	23 (15.8)	11 (12.0)	.71
Hospital mortality	46 (26.7)	31 (21.2)	22 (23.9)	.51
Cause of death†				
Shock	32 (69.6)	15 (48.4)	11 (50.0)	.16
Mechanical complications	7 (15.2)	4 (12.9)	3 (13.6)	.16
Other causes	7 (15.2)	12 (37.7)	8 (36.4)	.16

*LV indicates left ventricle. Values are expressed as number of cases and percentage of total numbers (n).
†Of total deaths.

(69.6% of deaths were due to cardiogenic shock in the untreated group vs 49.1% in treated patients; *P*=.04). There were 32 rehospitalizations (7.8%) over 1 month and total mortality increased to 24.9% with five deaths; 23% among the patients who received reperfusion therapy and 28.2% among those who did not (*P*=.23). There was no significant difference in hospital and 1-month mortality between the three treatment modalities (Table 4 and Figure 1).

Table 5 and Figure 2 show predictors of mortality at 1 month (univariable and multivariable analysis). Greater age, lower blood pressure at admission and, in particular, advanced Killip class were the predictors of 30-day mortality, but not the use of fibrinolytics or primary angioplasty.

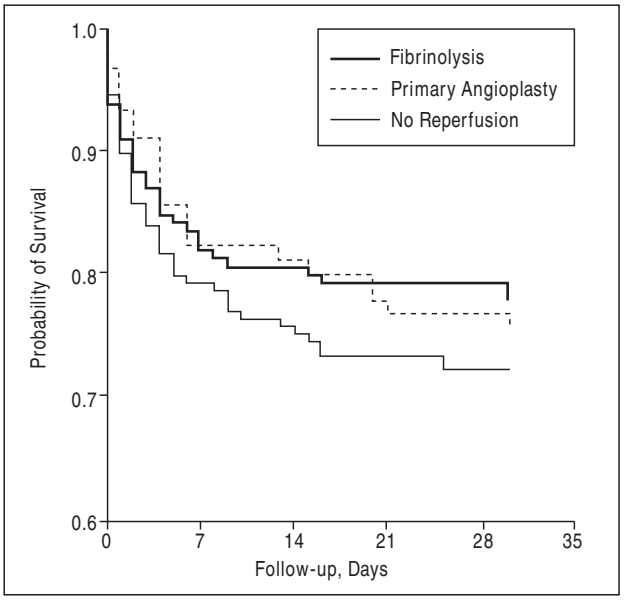

Figure 1. Survival curves of the 410 patients ≥75 years old included in the TRIANA 1 and 2 subregistries according to treatment received: fibrinolysis, primary angioplasty, or no reperfusion therapy.

DISCUSSION

The elderly AMI patients treated in Spanish hospitals with an active PA program are high-risk patients presenting a high rate of in-hospital complications associated with increased mortality. Despite this, almost half of these patients do not receive reperfusion thera-

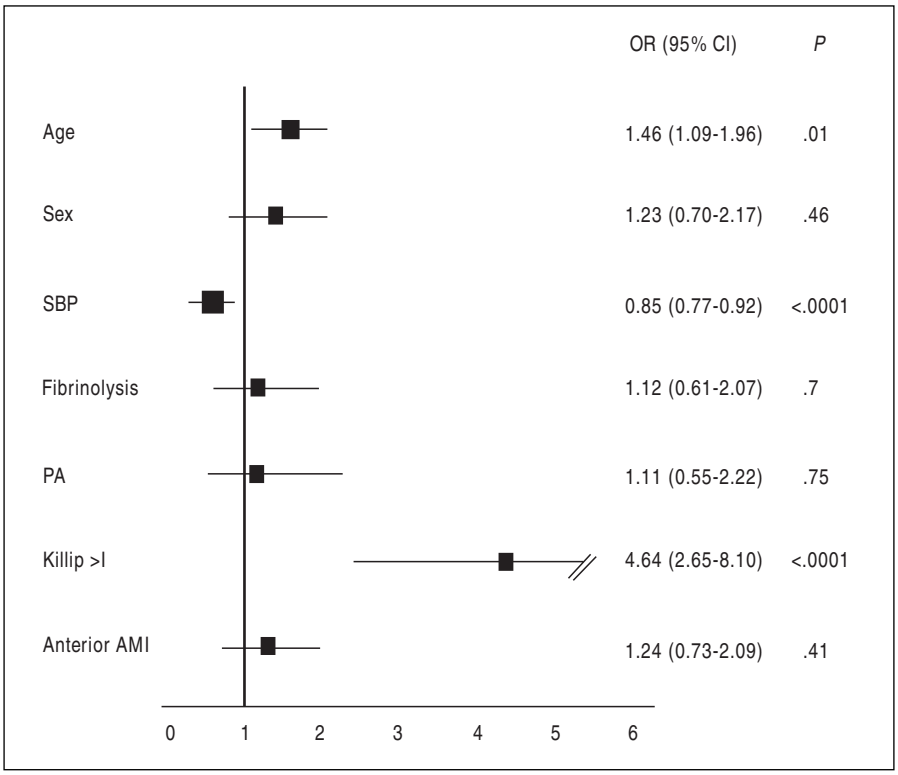

Figure 2. Independent predictors of 30-day mortality in the total population obtained via logistic regression.
OR indicates odds ratio; CI, confidence interval; SBP, systolic blood pressure; PA, primary angioplasty; AMI, acute myocardial infarction.

TABLE 5. **30-Day Mortality Predictors. Univariable Analysis***

	Survivors	Dead	*P*
Age, years	80	81.4	.006
Sex, male	75%	53%	.41
BP at admission, mm Hg	133	116	<.0001
Diabetes	74%	26%	.47
Current smoking habit	80%	20%	.59
Delay symptoms-hospital admission <6 h	75.2%	24.8%	.41
Killip class >1 at admission	58.8%	41.2%	<.0001
Anterior AMI	71.7%	28.3%	.11
No reperfusion/ fibrinolysis/angioplasty	71.8%/ 77.9%/75.6%	28.2% /22.1%/24.4%	.44
LVEF<40%	70%	30%	<.0001

*AMI indicates acute myocardial infarction; BP, blood pressure; LVEF, left ventricular ejection fraction.

py and most of those receiving it are treated with fibrinolysis.

This registry contains some data worthy of comment. On the one hand, the patients studied present similar characteristics to those described for this age group (high prevalence of diabetes, arterial hypertension, stroke, previous chronic kidney failure, and long delays before arrival at hospital, i.e., high-risk criteria) and, in fact, evolve unfavorably with a high incidence of complications and mortality during admission. However, the general management of these patients in Spanish hospitals, which we can consider as being elite centers from the viewpoint of therapeutic resources for AMI, does not seem to differ greatly from that in the general population.[14] Thus, 42% of the patients did not receive any reperfusion therapy, which in approximately half of these cases was due to the delay in hospital admission, but in 2 out of every 5 cases the reason for the lack of reperfusion was not given. Furthermore, a certain number of patients with other reported contraindications had been candidates for PA although not for fibrinolysis. Still more noteworthy is the fact that, in the hospitals with PA available, the reperfusion therapy of choice for the most elderly AMI patients is fibrinolysis, a fact which is quite difficult to explain. Although no definitive evidence exists regarding the ideal reperfusion therapy for elderly AMI patients, some evidence suggest that PA is probably better than fibrinolysis. It is known that PA is better than fibrinolysis in the general population and, in particular, in higher-risk patients.[15] In the only randomized study conducted specifically in patients >75 years old comparing PA with fibrinolysis, although this only included 77 patients over 4 years in a single hospital, there was a considerable reduction in early and long-term mortality in the patients treated with PA compared to those who received streptokinase.[11] These data are in line with other clinical trials and with observational studies which suggest that primary angioplasty specifically benefits elderly patients.[12,13-16] In addition, the efficacy of fibrinolysis in elderly patients is a matter of controversy, since

some published results suggest that it could be more effective in patients ≥75 years than in younger patients,[7] less effective[8] or could even be associated with greater 30-day mortality.[9-17] Most patients treated with fibrinolysis received tenecteplase, but the ideal fibrinolytic for elderly patients remains unknown. In the GUSTO I study, alteplase was associated with greater benefit than streptokinase, despite a slightly higher risk of stroke.[18] In the ASSENT 2 study, tenecteplase was slightly better than alteplase, especially in women >75 years old and in the patients who presented with a delay >4 h,[19] a frequent situation among the elderly. However, although the most widely used drug in our patients (tenecteplase) might have some advantages in this special population group, the ASSENT 3 Plus study demonstrated a prohibitive rate (6.7%) of intracranial hemorrhages in the patients >75 years old treated with tenecteplase and standard doses of enoxaparin.[20] Two-thirds of the patients in the TRIANA registry treated with tenecteplase received treatment with enoxaparin, which could explain the high rate of intracranial hemorrhages observed. The fundamental reason why fibrinolysis is the treatment of choice in elderly AMI patients in hospitals that employ primary angioplasty remains unknown since, in addition to their probable greater efficiency, these hospitals do not suffer the two main limitations to PA: logistic difficulties regarding its implementation and the team's lack of experience.

Finally, there was excessive delay before beginning reperfusion, especially regarding fibrinolysis, where the recommended 30 min was exceeded and even the time recorded in other series of Spanish hospitals was surpassed. The Acute Myocardial Infarction Hospital Registration Project (PRIAMHO II) showed that in patients with a mean age of 65.4 years in the year 2000 there was a median of 45 min[14] from the time of arrival at the emergency unit until fibrinolysis was done, which is slightly less time than that found in the TRIANA registry (48 min). In addition, the median door-guidewire time in the patients treated with PA was 90 min in our series, which compares negatively with the 80 min in the PRIAMHO II study. It is known that, in elderly patients, delays in arrival at the Emergency Unit is associated with a delay in establishing any reperfusion therapy when compared with younger patients,[21] even though they have greater absolute risk. The TRIANA study demonstrates that hospital delay in elderly AMI patients is also very high.

Clinical Implications

Elderly AMI patients treated in Spanish centers with active PA programs form a selected subgroup with a high rate of complications and mortality. The TRIANA registry data suggest deficiencies and inconsistencies in the treatment of AMI in patients ≥75 years old and highlights the pending issue concerning which reperfusion therapy is optimal in elderly patients. It provides valuable information regarding the feasibility of a study to compare both reperfusion therapy options.

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APPENDIX. **Researchers and Hospitals Participating in the TRIANA 1 and 2 Registries**

TRIANA 1. See p. 349.

TRIANA 2. N. Alonso, Complejo Hospitalario de León Hospital Princesa Sofía, León. J. Ángel, Ciudad Sanitaria Vall d'Hebron, Barcelona. J.J. Araiz, Hospital Clínico Universitario Lozano Blesa, Zaragoza. A. Bethancourt, Hospital Universitario Son Dureta, Palma de Mallorca. R. Blanco, Hospital de Cruces, Baracaldo. H. Bueno, Hospital General Universitario Gregorio Marañón, Madrid. F. Calvo, Hospital Do Meixoeiro, Vigo. R. Camarasa, Hospital General Universitari d'Alacant, Alicante. E. Esplugas, Ciudad Sanitaria y Universitaria de Bellvitge, L'Hospitalet de Llobregat, Barcelona. F. Fernández Avilés, Hospital Clínico de Valladolid, Valladolid. A. Fernández-Ortiz, Hospital Clínico San Carlos, Madrid. F. Hernández, Hospital 12 de Octubre, Madrid. J.M. Hernández, Hospital Virgen de la Victoria, Málaga. R. Hidalgo, Hospital Virgen de la Macarena, Sevilla. M. Jaquet, Hospital Clínico Universitario de Santiago, Santiago de Compostela. J. Martínez. Hospital de Navarra, Pamplona. L. Rodríguez Padial, Hospital Virgen de la Salud, Toledo. S. Romaní, Hospital Clínic, Barcelona. C. Romero, Hospital Universitario de la Princesa, Madrid. J. Romero, Fundación Jiménez Diaz, Madrid. F. Ruiz, Hospital Universitario Virgen de las Nieves, Granada. I. Sánchez, Hospital Central de Asturias, Oviedo. C. San José, Hospital Universitario Marqués de Valdecilla, Santander. C. Vázquez, Hospital Universitario Miguel Servet, Zaragoza. N. Vázquez, Hospital Juan Canalejo, A Coruña.

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